REMARKS/ARGUMENTS

Status of the Claims

Claims 91-93 and 97-98 have been canceled without prejudice to or disclaimer of the subject matter encompassed thereby. Applicants reserve the right to pursue these claims in a continuation application or to take other such appropriate action to seek protection of this canceled subject matter. Claims 34, 94, 96 and 99 have been amended to replace the phrase "host cell" with the phrase "plant cell." Support for these amendments can be found in previously presented claims 92-93 and 97-98. As such, no new matter has been added by way of these amendments.

Claims 30-34, 90, 94-96 and 99 are pending in the application. Reexamination and reconsideration of the pending claims are respectfully requested in view of the following remarks. The Examiner's rejections in the Office Action are addressed below in the order set forth therein.

Rejections of the Claims Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 30-34, 90-93 and 95-98 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Levy *et al.* (*Proc. Natl. Acad. Sci. USA* (1981) 78(10): 6186-6190) in view of U.S. Patent Publication No. US 2005/0221344 (hereinafter referred to as the '344 publication). This rejection of the claims is respectfully traversed.

Applicants' claimed invention is drawn to novel carboxy-terminal truncations of human alpha-2b-interferon, wherein the last eight residues of the human sequence are not present in either the precursor polypeptide encoded by SEQ ID NO:5 or the mature polypeptide encoded by SEQ ID NO:10. Such truncations are referred to herein as "delta-8" C-terminal truncations. The amended claims encompass these isolated polypeptides, isolated polynucleotides encoding such polypeptides, expression cassettes comprising these isolated polynucleotides, and plant cells comprising these expression cassettes.

The Levy *et al.* reference teaches the primary structures of three species of human interferon (alpha-1, alpha-2 and beta 1) that exhibit a 10 amino-acid carboxy-terminal truncation.

The '344 publication teaches rat and human precursor and mature "interferon-like" (IFN-L) polypeptides, the presence of leader sequences or signal peptides in such polypeptides, possible truncated versions of such polypeptides, polynucleotides encoding such polypeptides, vectors comprising such polynucleotides and host cells comprising such vectors. As the present claims are not rejected under 35 U.S.C. § 102(b), the Examiner acknowledges that neither of the cited references disclose the polypeptides, polynucleotides or other compositions of Applicants' claimed invention that are drawn to delta-8 C-terminal truncations of human alpha-2b-interferon.

The Office Action asserts that a person of ordinary skill in the art would have been motivated by the combined teachings of the Levy *et al.* reference and the '344 publication to create nucleic acid molecules encoding truncated human alpha-2b-interferon polypeptides equivalent to the polypeptides of SEQ ID NO:10 or SEQ ID NO:5. Furthermore, the Office Action asserts that, because there is a finite number of amino acids within the carboxy-terminus region of alpha-2b-interferon (*e.g.*, the 10 amino-acid C-terminal truncation taught by the Levy *et al.* reference), there is sufficient motivation provided by the Levy *et al.* reference to create additional alpha-2b-interferon truncation mutants for the purpose of studying the biological role of the carboxy terminus. As stated on page 4 of the current Office Action, if a person of ordinary skill pursues known options within his or her technical grasp and achieves *anticipated success*, it is likely the product not of innovation but of ordinary skill and common sense. Applicants respectfully submit that the delta-8 C-terminal truncation mutants of the claimed invention exhibit *unexpected results* over the cited prior art and are accordingly nonobvious.

Per *Graham v. John Deere Co.*, 383 U.S. 1 (1966), unexpected results are a secondary consideration that may tip the scales towards a conclusion of nonobviousness. Such unexpected results may include: **i)** greater than expected results, **ii)** superiority of a shared property, **iii)** presence of an unexpected property, and **iv)** absence of an expected property (see, MPEP § 716.02(a)). Applicants respectfully submit that the present invention is nonobvious in view of the cited prior art references, as the claimed delta-8 C-terminal truncations of human alpha-2b-interferon possess *unexpectedly superior biological activity* when compared to full-length human alpha-2b-interferon polypeptides and other C-terminal truncation mutants.

Such unexpected results are taught by U.S. Patent Application No. 11/874,607 (hereinafter referred to as the '607 application), which was supplied as Cite No. 14 on the PTO-1449 Form filed with the Supplemental Information Disclosure Statement dated March 9, 2009. The '607 application discloses comparative studies evaluating the effects of delta-7, delta-8 and delta-9 C-terminal truncations on alpha-2b-interferon anti-proliferative activity (see, page 30, Table 6) and antiviral activity (see, page 31, Table 7) when compared to a full-length recombinant human alpha-2b-interferon (rhIFNa2b) and a full-length World Health Organization alpha-2b-interferon reference control (WHO IFNa2b). Although the '607 application represents post-filing data, the results observed are inherent properties of the claimed polypeptides.

As demonstrated in Table 6 of the '607 application, the claimed delta-8 C-terminal truncation mutant possesses unexpectedly superior *anti-proliferative activity* when compared to both rhIFNa2b (39% greater specific activity) and WHO IFNa2b (91% greater specific activity). Furthermore, the results shown in Table 6 demonstrate that the delta-8 C-terminal truncation mutant is unexpectedly superior to other C-terminal truncation mutants. Specifically, the delta-8 C-terminal truncation mutant exhibits 24% greater specific activity than the delta-9 C-terminal truncation mutant. Table 7 of the '607 application demonstrates that the claimed delta-8 C-terminal truncation mutant also possesses unexpectedly superior *antiviral activity*, which is measured as the units per milliliter of interferon necessary to produce a cytopathic effect of 50% with Vesicular stomatitis virus (VSV) in MDBK cells. Although the delta-8 C-terminal truncation mutant has a potency comparable to WHO IFNa2b (4% lower), it is 39% more potent than rhINFa2b, 17% more potent than the delta-7 C-terminal truncation mutant, and 11% more potent than the delta-9 C-terminal truncation mutant. Thus, the specific delta-8 C-terminal truncation mutant exhibits unexpectedly superior anti-proliferative and antiviral activity when compared to full-length recombinant alpha-2b-interferon polypeptides and other C-terminal truncation mutants.

In addition to the biological activities disclosed in the '607 application, Applicants note that there is no teaching or suggestion in the cited references that specific C-terminal truncations would provide a technical advantage compared to full-length alpha-2b-interferon or other C-terminal truncation mutants. In fact, neither the delta-10 C-terminal truncation mutants taught by

the Levy *et al.* reference, nor the truncated versions of the IFN-like polypeptides taught by the '344 publication, are shown to possess any type of biological activity that is *greater than or equivalent to* a full-length alpha-2b-interferon or other C-terminal truncation mutant. Therefore, Applicants submit that it could not have been anticipated by a person of ordinary skill in the art that the claimed delta-8 C-terminal truncation mutants of alpha-2b-interferon would possess unexpectedly superior biological activity when compared to full-length alpha-2b-interferon polypeptides and other C-terminal truncation mutants.

Applicants remind the Examiner that, although the U.S. Supreme Court recently declined to permit a "rigid" application of the teaching-suggestion-motivation to combine (TSM) test to obviousness determinations, the Court did hold that the presence or absence of a teaching, suggestion, or motivation to combine the cited references provides a "helpful insight" regarding the obviousness of an invention. *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ2d 1385, 1389 (U.S. 2007). The Supreme Court went on to acknowledge the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in way the claimed invention does" in an obvious determination. *Takeda Chemical Industries, Ltd. V. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169, 1174 (Fed. Cir. 2007; citing *KSR Int'l Co. v. Teleflex, Inc.*). As discussed, neither the Levy *et al.* reference nor the '344 publication teach or suggest that creating delta-8 C-terminal truncation mutants of alpha-2b-interferon would provide superior biological activity compared to full-length alpha-2b-interferon, as neither reference discloses an example of *any* C-terminal truncation mutant having *equivalent or greater biological activity* than a full-length alpha-2b-interferon or another C-terminal truncation mutant. Therefore, there is no teaching, suggestion, or motivation in the cited references that would have prompted a person of ordinary skill in the relevant field to combine the elements in way the claimed invention does for the purpose of improving the biological activity of alpha-2b-interferon. Accordingly, Applicants respectfully request that the rejection of claims 30-34, 90-93 and 95-98 under 35 U.S.C. § 103(a) be withdrawn.

Claims 94 and 99 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Levy *et al.* reference in view of the '344 publication, and further in view of U.S. Patent No.

6,096,546 (hereinafter referred to as the '546 patent). This rejection of the claims is respectfully traversed.

The teachings of the claimed invention, the Levy *et al.* reference and the '344 publication are described above. The '546 patent teaches the use of duckweed cells for expressing recombinant proteins. The Office Action asserts that a person of ordinary skill in the art would have been motivated by the combined teachings of the cited references to achieve the compositions of claims 94 and 99.

As discussed herein above, Applicants respectfully submit that the present invention is nonobvious in view of the cited prior art references, as the claimed delta-8 C-terminal truncation mutants of alpha-2b-interferon possess *unexpectedly superior biological activity* compared to full-length human alpha-2b-interferons and/or other C-terminal truncation mutants. Additionally, neither the delta-10 C-terminal truncation mutants taught by the Levy *et al.* reference, nor the truncated versions of the IFN-like polypeptides taught by the '344 publication, are shown to possess any type of biological activity that is *greater than or equivalent to* a full-length alpha-2b-interferon or other C-terminal truncation mutants. Therefore, it could not have been anticipated by a person of ordinary skill in the art that the claimed delta-8 C-terminal truncation mutants of alpha-2b-interferon would possess unexpectedly superior biological activity when compared to control alpha-2b-interferon and other C-terminal truncation mutants. As the '546 patent only teaches the use of duckweed cells as an expression system for recombinant proteins, it also does not teach that delta-8 C-terminal truncation mutants would be expected to have superior biological activity when compared to full-length alpha-2b-interferon and other C-terminal truncation mutants. Accordingly, Applicants respectfully request that the rejection of claims 94 and 99 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSIONS

In view of the foregoing remarks and amendments, the Examiner is respectfully requested to withdraw the rejections made to the pending claims. Applicants respectfully submit that this application is now ready for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefor (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES PATENT & TRADEMARK OFFICE ON NOVEMBER 3, 2010.